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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/594,577	06/15/2000	Hideaki Hosokawa	000683	8983

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	**Application No.**	**Applicant(s)**	
	09/594,577	HOSOKAWA ET AL.	
	Examiner	**Art Unit**	
	Gary B. Nickol Ph.D.	1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

THE REPLY FILED 02 October 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ they raise the issue of new matter (see Note below);
   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____.
3. ☐ Applicant's reply has overcome the following rejection(s): _____.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See attached*.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *31-35 and 37-44*.

   Claim(s) withdrawn from consideration: _____.
8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.
10. ☐ Other: _____

Response to Amendment

The Amendment filed October 2, 2003 in response to the Final Rejection mailed July 2, 2003 is acknowledged and has been entered.

Claims 1-30 and 36 are cancelled.

Claims 31-35 and 37-44 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

Claims 31-33 and 37-44 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record with regards to the modes of detection as set forth in Paper No. 14. The written description is not commensurate in scope with the claims because there is no clear support for merely detecting cancer by using a certain quantity of proteins that bind to sugar chain structures on CEA molecules. The written description is based on the ratio of the amount of the CEAs having a specific sugar chain structure relative to the total amount of CEAs in the sample compared to normal human being samples wherein said anti-sugar proteins require the addition of *all* four antibodies to S-Le^a, S-Le^x, Le^a and Le^y (Table I), not merely two or three proteins in some instances.

Applicants argue that the Examiner has mischaracterized the claims because the term

"ratio" and the value of this ratio are not recited in the claims. Applicants add that the claims recite detection or non-detection of complexes corresponding to the different CEAS. This argument has been considered but is not found persuasive. The fact that a ratio is not recited in the claims is indicative of the lack of a written description with regards to the claimed invention. The written description, in this case, for *detecting cancer* is not based merely on detection or non-detection of complexes. As set forth previously, the ability to detect a specific type of cancer is much more quantitative. It is based on the ratio (%) of the amount of the CEAS having a specific modified sugar chain structure relative to the amount of total CEAS (see page 9, 24, and 27 of the specification). Applicants further argue that it is unclear what is meant by "need" in the statement that "only ONE antibody **need** be detected" and it is not stated why need is relevant here. However, applicant's amendment (Claim 39) appears to have addressed this problem. Thus, in review, applicant's arguments have not all been found persuasive and the rejection is maintained.

Claims 31-35 remain rejected under 35 U.S.C. 112, first paragraph, for the reasons of record because the specification, while being enabling for a method for detecting cancer comprising:

1. Adding to a sample an antibody to a constant region of CEA

2. Adding to said sample a first protein which selectively binds to a sugar chain structure on CEA, said first protein is selected from the group consisting of Anti-Le^a antibody, Anti-S-Le^x antibody, Anti-S-Le^a antibody and Anti-S-Le^y antibody,

3. Adding to said sample, a second protein which selectively binds to a second sugar chain structure on CEA different from said first protein wherein said second protein is selected from the group consisting of Anti-Le^a antibody, Anti-S-Le^x antibody, Anti-S-Le^a antibody and Anti-S-Le^y antibody.

4. Adding to said sample, a third protein which selectively binds to a third sugar chain structure on CEA wherein said third protein is different from said first and second protein and wherein said third protein is selected from the group consisting of Anti-Le^a antibody, Anti-S-Le^x antibody, Anti-S-Le^a antibody and Anti-S-Le^y antibody.

5. Adding to said sample, a fourth protein which selectively binds to a fourth sugar chain structure on CEA wherein said fourth protein is different from said first, second, and third protein, and wherein said fourth protein is selected from the group consisting of Anti-Le^a antibody, Anti-S-Le^x antibody, Anti-S-Le^a antibody and Anti-S-Le^y antibody.

6. Determining the presence of a cancer in said sample based on a ratio of the amount of the CEAs having a specific sugar chain structure relative to the total amount of CEAs in the sample compared to normal human being samples.

does not reasonably provide enablement for the method as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicants argue that the claims are already enabled as set forth by the working examples in the specification. Applicants further point out that while some lectins or anti-sugar chain antibodies might not be bind to any CEAS, it would not affect the ability of one of skill in the art

to carry out the method as claimed. Applicants add that the method as claimed involves only adding these proteins, detecting the product, and determining a diagnosis based on this detection. Applicants further argue that the selection of appropriate lectins and anti-sugar chain antibodies (other than those listed in the specification) for medically useful detection methods can be made without undue experimentation. Applicants add that, for example, lectin or antibody selection can be made rationally from known information on types of CEAS present in cancer, which would require almost no experimentation. Alternatively, applicants argue that the testing of different lectins against known cancer samples to determine which would be useful would be straightforward and would not represent undue experimentation.

These arguments have been carefully considered but are not found persuasive. Applicants have simply argued the opposite in the absence of clear and convincing evidence to suggest that the *broadly* claimed subject matter would predictably detect cancer according to the method as claimed. Furthermore, the guidance necessary to detect a particular type of cancer is highly specific to the determined **ratio** of specific anti-sugar chain antibodies relative to the total amount of CEAs. Thus, the scope of the presently claimed subject matter does not appear to encompass methods for detecting cancer because merely detecting complexes of different anti-sugar chain moieties in combination with an antibody to a constant region of CEA is not disclosed. Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
December 2, 2003